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Does LENT prognostic score predict mortality? An observational study

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Abstract

Aim: Determining the patients with long survival helps determine the best prevention strategies such as pleurodesis or tunneled pleural catheter, providing better palliation by minimizing the symptoms and morbidities associated with MPE relapse. This study aims to evaluate the predictive strength of LENT, a current prognostic score for MPE patients, and determine its effect on survival and importance in clinical decision-making.

Material and Methods: MPE patients between 2008 and 2020 were examined retrospectively. Age, sex, type of cancer, histological type, LDH, blood Neutrophil/Lymphocyte values were taken, and ECOG, biopsy, and survival rates were calculated. Survival time was calculated as the period between thoracentesis result and death.

Results: The study group consisted of 268 MPE patients, and the average age of patients was 65.3±13.2 years, and 58.2% of the patients were male. Patients with high-risk LENT scores were observed to have 2.8 times more risk compared to the low-risk patients within the period of observation (Hazard Ratio:2.836, p:0.001). The median survival time for moderate-risk patients was shorter than for low-risk group (450 vs. 623 days).

Discussion: The LENT prognostic score is a simple score that can be used on patients suitable for pleural fluid analysis and significantly better than the Eastern Cooperative Oncology Group performance score (ECOG PS) for predicting survival. It is considered to be used conveniently to guide MPE treatments.

Keywords

ECOG, Lung Cancer, Malign Pleural Effusion, Survival

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Introduction

Malign pleural effusion (MPE) is the presence of malign cells in pleural fluid and/or parietal pleura [1]. MPE occurs in around 15% of all cancer patients [2]. Approximately 75% of MPE is caused by breast and lung metastases, while only 40% are caused by lung cancer. Moreover, pleural effusion is present in around 15% of lung cancer cases at the time of initial diagnosis [3].

The presence of MPE reduces life expectancy significantly [3]. Although it depends on the type of the underlying malignity, the median survival after diagnosis is specified as 3 to 12 months in guidelines [4]. Correct evaluation of MPE is crucial for planning suitable treatment to achieve the highest benefit for the survival of the patient and to keep the damage at minimal levels [5].

Since they might cause morbidities as well as hospitalization, the treatments applied might cause additional load for patients, loss of life quality and additional costs in health expenditures. Determining the patients with the worst survival has the potential to help increase the quality of life for these patients by focusing on reducing the hardships they experience in their remaining lives. In addition, determining the patients with better survival helps determine good prevention strategies such as pleurodesis or tunneled pleural catheter, providing good palliation by minimizing symptoms and morbidities associated with MPE relapse. The critical point here is to determine which patients will achieve this survival [6]. Therefore, the correct prognostic evaluation of the patients becomes more important. For this purposes, various factors predict negative survival of patients with MPE [3, 7, 8]: high pleural fluid lactate dehydrogenase (LDH; >1,500 IU/L), Eastern Cooperative Oncology Group (ECOG) performance score (3–4), high blood neutrophil: lymphocyte rate (>9), cancer type (lung), low pleural fluid pH (<7.28) and high sVEGFR-1 pleural fluid level (9-13).

LENT score (Serum Lactate dehydrogenase (LDH), ECOG PS, blood Neutrophil/Lymphocyte Ratio, tumor type) is a combined scoring method, created when searching for a stronger predictor for oncology cases where malign pleural fluid occurs [2]. The score categorizes patients as low-, moderate-, or high-risk groups based on their survival time. It is reported that 97% of the high-risk group patients, categorized using the LENT scoring system died within six months [2].

This study aims to evaluate the predictive strength of LENT, a current prognostic score for MPE patients and to determine its effect on survival and importance in clinical decision-making. Moreover, it is further aimed to compare the LENT score with ECOG, a traditional but subjective scoring system.

Material and Methods

Study Population and Data Collection

MPE patients between 2015 and 2020 were examined retrospectively. Malign cells of the patients were confirmed with pleural fluid or pleural biopsy. Malign cells were analyzed using conventional cytology using biopsy material and histology analyses were conducted. Ethics committee approval for the study was obtained from the Ondokuz Mayıs University Clinical Trials Ethics Committee, with no. 2020/150.

Measurements

Basal prognostic clinical and laboratory examinations were taken from the hospital's electronic registry system. Age, sex, type of cancer, histological type, LDH, blood Neutrophil/Lymphocyte values were taken and ECOG, biopsy, survival rates were calculated. Survival time was calculated as the period between thoracentesis result and death. LENT score was classified as low (0-1), moderate (2-4) and high (5-7) in line with the literature [2]. Performance scores of the patients were calculated using ECOG-PS.

Statistical Analysis

SPSS v21 (Chicago, US) was used for statistical analyses. For the complementary analyses, average, median and percentage distributions are utilized. ROC curves were used for survival analyses, areas under curves (AUC) were shown. Sensitivity and specificity values at the cut-off points were chosen according to Youden Index. Kaplan-Meier curve and Cox regression analyses were used for survival and hazard ratio. AUC was calculated for the 1-, 3-, 6-, 12-month periods and overall survival. $P<0.050$ was considered statistically significant.

Results

The study group consisted of 268 MPE patients, the average age of patients was 65.3±13.2 years, and 58.2% of the

Table 1. Sociodemographic and clinical characteristics of the patients

		Mean±SD (%)	n
Age		65.3±13.2	268
Sex	Male	58.2	156
	Female	41.8	112
Cancer Type	Lung	39.2	105
	Gastrointestinal	22.8	61
	Hematological	11.2	30
	Breast	10.8	29
	Gynecoid	7.1	19
	Other	5.6	15
	Mesothelioma	3.0	8
Histological Type	Adenocarcinoma	42.9	115
	Metastatic carcinoma	40.3	108
	Squamous cell carcinoma	10.4	28
	Small cell lung carcinoma	4.5	12
LDH (U/L)	<1500	89.2	239
	>1500	10.8	29
Neutrophil/Lymphocyte	<9	70.9	190
	>9	29.1	78
ECOG-PS	0	0.7	2
	1	54.9	147
	2	28.4	76
	3	12.3	33
	4	3.7	10
LENT score	0-1-Low	7.8	21
	2-4 Moderate	70.5	189
	5-7 High	21.6	58
Exitus	Present	86.9	233
	Absent	13.1	35

LDH: lactate dehydrogenase, ECOG-PS: Eastern Cooperative Oncology Group (ECOG) performance score, LENT: LDH, ECOG performance score, blood neutrophil/lymphocyte ratio, tumor type

Table 2. ROC curve values for LENT score and ECOG PS for predicting mortality

	Cut-off	AUC	Std. Error	95% CI		P value	Sensitivity	Specificity
				Lower	Upper			
LENT Score								
Overall survival	>4	0.624	0.043	0.514	0.708	0.018*	24.9%	100%
Mortality 1 month	>4	0.618	0.078	0.465	0.770	0.115	43.8%	78.8%
Mortality 3 months	>4	0.610	0.049	0.514	0.706	0.020*	40.0%	82.1%
Mortality 6 months	>4	0.610	0.038	0.525	0.676	0.007*	35.2%	84.9%
Mortality 12 months	>4	0.589	0.035	0.520	0.657	0.012*	30.8%	87.0%
ECOG PS								
Overall survival	>2	0.637	0.044	0.551	0.724	0.009*	47.2%	75.3%
Mortality 1 month	>2	0.549	0.071	0.510	0.688	0.510	56.3%	52.3%
Mortality 3 months	>2	0.625	0.008	0.535	0.714	0.008*	64.4%	60.0%
Mortality 6 months	>2	0.583	0.037	0.510	0.656	0.027*	20.6%	86.1%
Mortality 12 months	>2	0.555	0.035	0.486	0.624	0.118	19.2%	87.0%

Note: AUC: Area under the curve, CI: Confidence interval, ECOG PS: Eastern Cooperative Oncology Group (ECOG) performance score (PS).

Table 3. Survival analysis of 1, 3, 6, and 12 months according LENT Scores

LENT Score	0-1 Low	2-4 Moderate	5-7 High
Survival 1 month	95.2	95.8	87.9
Survival 3 months	95.2	86.2	69.0
Survival 6 months	81.0	72.0	46.6
Survival 12 months	76.2	55.0	31.0
Survival Overall	33.3	14.8	0.0

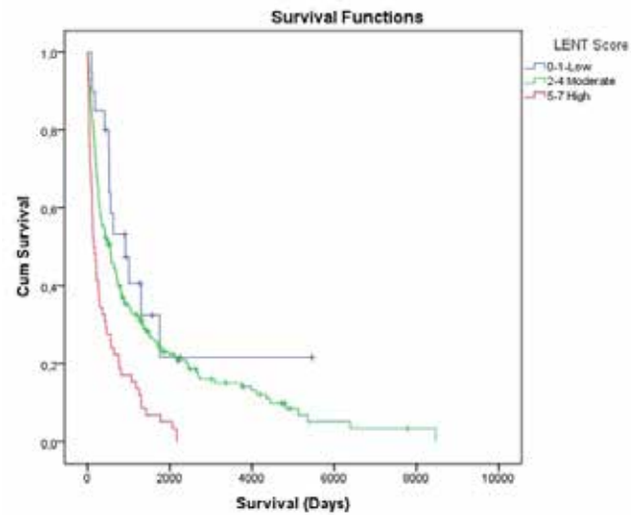

Figure 1. Kaplan Meier survival Analysis according to LENT Scores

patients were male. Among the patients, 39.2% had lung, 22.6% gastrointestinal and renal, 11.2% had hematologic cancer. When the cancers were examined histologically, the most common type was adenocarcinoma (42.6%). During the examined period, 86.9% of the patients were passed away. The socio-demographic characteristics of the patients are presented in Table 1.

When the cut-off point is taken as 4 for the LENT score and 2 for ECOG-PS, the AUC value was found to be 0.624 for the LENT score (p:0.018, sensitivity: 24.9%, specificity 100%) and 0.637 for the ECOG-PS score (p:0.009, sensitivity: 47.2%, specificity 75.3%). It was observed that the LENT score had higher predictivity values for 1-, 6-, and 12-month periods compared to the ECOG-PS score. Table 2 presents the ROC curve values for LENT score and ECOG PS for predicting mortality.

When the 1-, 3-, 6-, and 12-month survival of LENT score groups is examined, it was observed that 33.3% of the low-risk group, 14.8% of the moderate-risk group, and 0.0% of the high-risk group survived. In the 12-month survival period, the survival rates were 76.2%, 55.0%, and 31.0% for the low-, moderate-, and high-risk groups, respectively. Table 3 presents the survival rates for 1-, 3-, 6-, and 12-month periods based on LENT scores.

The median survival time among the LENT score groups was 623 days, 450 days, and 165 days for the low-, moderate-, and high-risk groups, respectively.The Kaplan-Meier survival analysis is presented in Figure 1. The Cox regression model for the LENT score groups in predicting survival in all patients was statistically significant (x^2:27.763, df:2, p:0.001). Patients with high-risk LENT scores were observed to have 2.8 times more risk compared to low-risk patients within the period of observation (Hazard Ratio:2.836, p:0.001). The median survival time of the moderate risk patients was shorter compared to the low-risk group (450 vs. 623 days); however, the risk between these two groups was not considered significant for this model (Hazard Ratio:1.333, p:0,304).

Discussion

In our study, we evaluated the performance of the LENT score in predicting prognosis for patients with MPE. We found out that survival in patients with high LENT scores was shorter. We determined that the LENT score predicts survival in patients with MPE. Taking the predictive values of our study, we observed that the LENT score was higher than the ECOG-PS score for the 1-, 6-, and 12-month periods. Gayaf et al. reported that although the LENT score is equal or superior to the ECOG in terms of predicting survival for 1- or 3-month, the difference decreases in the long-term survival analyses and that the LENT score has almost the same effect as the ECOG PS for overall survival [9].

When the cut-off point is taken as 4 and 2 for the LENT score and ECOG-PS respectively in our study, it was found out that the sensitivity and specificity for the LENT score were 24.9% and

100%, respectively. In another study, it was demonstrated that sensitivity and specificity were 69.8% and 100%, respectively, when the LENT score is >4 [9]. Similarly, our study indicates that the LENT score has a higher specificity and that lower LENT scores can be utilized in clinical practice.

According to our evaluations, median survival times were 623, 450 and 165 days for the low-, moderate-, and high-risk groups in the LENT score chart, respectively. Survival times in the study by Clive et al. were 319, 130, and 44 days, respectively [2]. In the study by Gayaf et al., the median survival times were 662, 119, and 33 days for the low-/moderate-/high-risk groups according to the LENT score, respectively [9]. The most important reason for the longer median survival time in our study compared to other studies is that the patients receiving immunotherapy or other targeted therapies were not excluded. Particularly, it was demonstrated that the survival periods are longer in the lung adenocarcinoma-induced MPE patients who receive treatment with tyrosine kinase inhibitors [10]. In the study by Abisheganaden et al., which had similar results to our research, it was shown that the median survival time of the high-risk patients with LENT score ≥5 (n = 36) was 190.5 days and that more than half of the patients (52.7%) survived for more than six months, while the median survival time of the moderate-risk patients with LENT score 2-4 (n = 34) was 346 days, and 70.5% of these patients survived for more than six months. In the current study, more than half of the patients with EGFR mutation with MPE from lung adenocarcinoma received tyrosine kinase inhibitor treatment [6].

In our study, the Cox regression analysis showed that the LENT score predicted survival in all patients. Patients with high-risk LENT scores were observed to have 2.8 times more risk compared to the low-risk patients within the period of observation. Although the median survival time of moderate-risk patients is shorter compared to the low-risk patients, the risk between these two groups was not statistically significant. In the Cox regression analysis conducted by Gayaf et al., it was shown that there is a significant difference in terms of survival between the moderate and high-risk groups according to the LENT score [9].

Our findings support that the high pleural LDH ratio, which demonstrates localized, acute inflammation, necrosis and cell death in pleural space, is a sign of poor prognosis in malign pleural effusions [11, 12]. Further, some studies proved that the leucocyte subtypes such as neutrophil and lymphocyte counts show the severity of the systemic inflammatory response in cancer patients [13]. In these studies, it was reported that increased serum NLR (neutrophil-lymphocyte ratio) has an adverse effect on overall survival [14]. In a study conducted to predict the survival among patients, it was found out in the multivariate analyses that the serum NLR is a distinct prognostic factor in the patients with MPE and the LENT prognostic score on its own has distinctly higher accuracy compared to the ECOG PS [2]. Since these ratios can be simply calculated in complete blood counts and available at a reasonable cost universally, it increases the value of ratios as biomarkers. Similarly, another study found out that the serum and pleural fluid NLR in lung cancer patients with MPE have an adverse effect on overall survival [15]. It was found out that the survival time is shorter in patients with high LENT scores and longer compared to the values in the ECOG-PS when predictive values for 1-, 6-, and 12-month periods were examined. We believe that, while the LDH and NLR ratios are guiding lights in determining a prognosis, their use in conjunction with the ECOG and tumor type is a better indicator of prognosis.

Our study has certain limitations. Firstly, patients receiving immunotherapy or other targeted therapies were not excluded. Although this inclusion led to an increase in survival periods in our study, it is considered that this situation does not prevent the use of the LENT score for predicting prognosis. Another limitation is that there are missing data regarding whether the effusions were newly diagnosed malign diseases or the presence of recurring/progressive conditions, or any previous treatment for malignity at the time of calculations for the LENT scores. In the literature, there is only one study on whether effusions represent a new malignant diagnosis or a recurring/progressive disease. In this study, no statistically significant difference was found between the progressive disease vs. newly diagnosed disease in the single variant Cox model [2].

Conclusion

The LENT prognostic score is a simple score that can be used in patients suitable for pleural fluid analysis and significantly better than the ECOG PS for predicting survival. It is considered to be used conveniently to guide MPE treatments.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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